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Original Contribution

Ovarian Cancer Risk Factors in African-American and White Women

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Ovarian cancer is the most lethal gynecologic malignancy in both African-American and white women. Although prevalences of many ovarian cancer risk factors differ markedly between African Americans and whites, there has been little research on how the relative contributions of risk factors may vary between racial/ethnic groups. Using data from a North Carolina case-control study (1999–2008), the authors conducted unconditional logistic regression analyses to calculate odds ratios and 95% confidence intervals for ovarian cancer risk factors in African-American (143 cases, 189 controls) and white (943 cases, 868 controls) women and to test for interactions by race/ethnicity. They also calculated attributable fractions within each racial/ethnic group for the modifiable factors of pregnancy, oral contraceptive use, tubal ligation, and body mass index. Many risk factors showed similar relations across racial/ethnic groups, but tubal ligation and family history of breast or ovarian cancer showed stronger associations among African Americans. Younger age at menarche was associated with risk only in white women. Attributable fractions associated with tubal ligation, oral contraceptive use, and obesity were markedly higher for African Americans. The relative importance of ovarian cancer risk factors may differ for African-American women, but conclusions were limited by the small sample. There is a clear need for further research on etiologic factors for ovarian cancer in African-American women.

African Americans; case-control studies; ovarian neoplasms

Abbreviations: BMI, body mass index; CI, confidence interval.

Ovarian cancer is the eighth most common cancer among both white and African-American women and the fifth most common cause of cancer death in the United States (1, 2). African-American women have lower incidence rates than white women (10.1 cases/100,000 women vs. 14.1 cases/100,000 women) but poorer 5-year survival (1). Despite the importance of ovarian cancer as a major cause of morbidity and mortality, there has been very little research on ovarian cancer among African Americans. Only 2 published papers have focused on risk factors for ovarian cancer among African Americans: 1 on a case-control study with 84 cases (3) and 1 on a multicenter analysis of 7 case-control studies involving 110 cases (4). Both of these reports had findings that were consistent with the major reproductive risk factors identified in white women, including inverse associations with parity and oral contraceptive use (3, 4), but some racial/ethnic differences were noted, including the absence of a protective effect for breastfeeding and no increased risk associated with a family history of ovarian cancer among African Americans (3).

As has been reported by John et al. (4), Ness et al. (3), and other authors (5–12), the prevalence of many factors associated with risk of ovarian cancer varies markedly between African Americans and whites. African-American women tend to have a greater number of pregnancies (5, 7), a higher prevalence of tubal ligation (6), a lower prevalence of endometriosis (9), and less use of menopausal hormones (5, 10), all of which would be associated with a lower incidence of ovarian cancer. They also tend to have an earlier age at menarche (11), are more likely to be obese (12), and are less likely to breastfeed (8), which could contribute to higher risk of ovarian cancer. Because most epidemiologic

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studies of ovarian cancer have enrolled very few African-American women, there is little information on the relative importance of these risk factors among African-American women as compared with white women and the extent to which differences in the prevalence of established risk factors can explain the lower incidence of ovarian cancer among African Americans.

In this paper, we use data from the North Carolina Ovarian Cancer Study to compare risk factors for ovarian cancer among African-American and white women. We also calculate population attributable fractions for risk factors that are both modifiable and show considerable racial/ethnic differences in prevalence to evaluate the relative proportions of cases in African-American and white women that are associated with these factors.

MATERIALS AND METHODS

The North Carolina Ovarian Cancer Study was a population-based, case-control study of epithelial ovarian cancer that was conducted in a 48-county region of North Carolina between 1999 and 2008. Newly diagnosed cases of epithelial ovarian cancer were identified through the North Carolina Central Cancer Registry using a rapid case ascertainment system. Pathology reports for eligible cases were sent to the study office at Duke University Medical Center, and consent to contact the women was requested from the treating physicians. Eligible cases were aged 20–74 years at diagnosis, had no prior history of ovarian cancer, resided in the study area, and were cognitively able to give consent and to complete an interview in English. All cases underwent standardized histopathologic review by the study pathologist for confirmation of the diagnosis. Control women were frequency-matched by age and race/ethnicity to the cases and were recruited from the same geographic region using list-assisted random digit dialing. The eligibility criteria were the same as those for the cases; in addition, the controls could not have had a bilateral oophorectomy.

The response rate among the cases was 66.5%, with nonparticipation being due to death (4.0%), debilitating illness (2.6%), physician refusal (4.7%), patient refusal (11.5%), or an inability to locate the patient (10.7%). Among potential controls, screening for eligibility could not be completed for 14% of phone numbers. Seventy-three percent of potential controls who passed eligibility screening agreed to be sent information about the study, and 60.1% of those consented to be in the study. Nonparticipation was due to refusal (27.4%) or an inability to contact the person (8.8%). Response rates were lower for African Americans than for whites (56.6% and 68.3%, respectively, for cases and 49.7% and 63.7%, respectively, for controls).

A total of 1,114 cases were enrolled, of whom 943 (84.6%) were white, 143 (12.8%) were African-American, and 28 (2.5%) were of other races/ethnicities. Among the 1,086 controls, 868 (79.9%) were white, 189 (17.4%) were African-American, and 29 (2.7%) were of other races/ethnicities. The analyses in this report were limited to women whose self-reported race/ethnicity was either white or African-American. The study protocol was approved by the Duke University Medical Center Institutional Review Board and by the human subjects committees at the North Carolina Central Cancer Registry and each hospital where cases were identified.

Table 1. Clinical and Histologic Characteristics of Epithelial Ovarian Cancer Cases in African-American and White Women, North Carolina Ovarian Cancer Study, 1999–2008

	Whites		African Americans		*P* Value[a]
	No.	%	No.	%	
All cases	(*n* = 943)		(*n* = 143)		
Invasive tumor	746	79.4	111	77.6	0.64
Low-malignant-potential tumor	194	20.6	32	22.4	
Missing data	3		0		
Invasive cases only	(*n* = 746)		(*n* = 111)		
Histologic type					
Serous	419	56.2	67	60.4	0.05
Clear-cell	82	11.0	2	1.8	
Endometrioid	116	15.5	19	17.1	
Mucinous	39	5.2	6	5.4	
Other	90	12.1	17	15.3	
Stage					
I or II	245	33.1	25	22.7	0.04
III or IV	496	66.9	85	77.3	
Missing data	5		1		
Grade					
Well-differentiated	93	12.9	18	16.8	0.12
Moderately differentiated	197	27.2	36	33.6	
Poorly differentiated or undifferentiated	433	59.9	53	49.5	
Missing data	23		4		

[a] *P* values were derived from chi-squared analyses.

Nurse-interviewers conducted in-person visits at which they obtained written informed consent, administered a 90-minute questionnaire, drew a blood sample, and performed anthropometric measurements (height, weight, and waist and hip circumferences). Information obtained with the questionnaire included family history of cancer; menstrual characteristics such as age at menarche and cycle length; reproductive history, including age at each pregnancy, pregnancy duration and outcome, and duration of breastfeeding; type, timing, and duration of hormone and contraceptive use; and lifestyle characteristics such as smoking history, alcohol consumption during the 5 years before interview, and physical activity. A life-events calendar, which marked milestones such as marriages and births, was used to aid recall of reproductive history and hormone use. Pictures of oral contraceptives, menopausal hormones, and certain other medications were also used to assist with recall.

Statistical analysis

Chi-squared analyses were used to compare clinical and histologic characteristics of cases between African Americans

Table 2. Characteristics of Invasive Epithelial Ovarian Cancer Cases and Controls, by Race/Ethnicity, North Carolina Ovarian Cancer Study, 1999–2008

	Whites						African Americans					
	Cases (n = 746)		Controls (n = 868)		OR[a]	95% CI	Cases (n = 111)		Controls (n = 189)		OR[a]	95% CI
	No.	%	No.	%			No.	%	No.	%		
Age, years												
20–39	38	5.1	81	9.3			11	9.9	22	11.6		
40–49	136	18.2	170	19.6			23	20.7	46	24.3		
50–59	239	32.0	261	30.1			37	33.3	67	35.4		
60–69	232	31.1	240	27.6			31	27.9	40	21.2		
70–74	101	13.5	116	13.4			9	8.1	14	7.4		
Age at menarche, years												
<12	181	24.4	157	18.2	1.00	Referent	28	25.5	53	28.0	1.00	Referent
≥12	562	75.6	708	81.8	0.67	0.53, 0.86	82	74.5	136	72.0	1.08	0.63, 1.85
Missing data	3		3				1		0			
No. of pregnancies								11				
0	120	16.1	87	10.0	1.00	Referent	14	12.6	11	5.8	1.00	Referent
1–2	319	42.8	348	40.1	0.62	0.45, 0.85	31	27.9	71	37.6	0.34	0.14, 0.82
≥3	307	41.2	433	49.9	0.45	0.33, 0.62	66	59.5	107	56.6	0.44	0.19, 1.05
P-trend					<0.0001		0		0			0.25
Age at first pregnancy, years												
<20	173	27.6	202	25.9	1.00	Referent	56	58.3	94	52.8	1.00	Referent
20–24	276	44.1	333	42.7	0.93	0.72, 1.21	30	31.3	52	29.2	0.98	0.56, 1.72
25–29	137	21.9	151	19.4	1.09	0.80, 1.49	8	8.3	19	10.7	0.73	0.30, 1.79
30–34	31	5.0	79	10.1	0.50	0.31, 0.79	1	1.0	10	5.6	0.18	0.02, 1.45
≥35	9	1.4	14	1.8	0.77	0.33, 1.84	1	1.0	3	1.7	0.65	0.07, 6.45
Missing data	120		89				15		11			
P-trend					0.0004							0.15
Age at last pregnancy, years												
<20	19	3.0	18	2.3	1.00	Referent	11	11.7	13	7.3	1.00	Referent
20–24	134	21.4	147	18.9	0.79	0.39, 1.57	24	25.5	35	19.8	0.82	0.31, 2.14
25–29	233	37.3	258	33.1	0.76	0.38, 1.49	25	26.6	51	28.8	0.57	0.22, 1.45
30–34	161	25.8	230	29.5	0.60	0.30, 1.18	22	23.4	48	27.1	0.54	0.21, 1.40
≥35	78	12.5	126	16.2	0.53	0.26, 1.08	12	12.8	30	16.9	0.43	0.15, 1.23
Missing data	121		89				17		12			
P-trend					<0.0001							0.04
Ever breastfeeding												
No	521	69.8	542	62.4	1.00	Referent	75	67.6	135	71.4	1.00	Referent
Yes	225	30.2	326	37.6	0.73	0.59, 0.90	36	32.4	54	28.6	1.16	0.69, 1.93
Missing data	0		0				0		0			
Tubal ligation												
No	559	75.0	579	66.8	1.00	Referent	77	69.4	93	49.2	1.00	Referent
Yes	186	25.0	288	33.2	0.68	0.54, 0.84	34	30.6	96	50.8	0.43	0.26, 0.71
Missing data	1		1				0		0			
Duration of oral contraceptive use, years												
Never use	244	34.5	239	28.3	1.00	Referent	47	43.9	58	32.2	1.00	Referent
<1	99	14.0	92	10.9	1.09	0.77, 1.52	15	14.0	14	7.8	1.36	0.59, 3.14
1–<5	166	23.4	228	27.0	0.75	0.57, 0.99	24	22.4	57	31.7	0.54	0.28, 1.04
≥5	199	28.1	285	33.8	0.73	0.55, 0.96	21	19.6	51	28.3	0.53	0.27, 1.03
Missing data	38		24				4		9			

Table continues

Table 2. Continued

	Whites						African Americans					
	Cases (n = 746)		Controls (n = 868)		OR[a]	95% CI	Cases (n = 111)		Controls (n = 189)		OR[a]	95% CI
	No.	%	No.	%			No.	%	No.	%		
Use of menopausal hormones												
No	276	37.0	456	52.6	1.00	Referent	75	68.8	148	78.3	1.00	Referent
Yes	470	63.0	411	47.4	1.85	1.50, 2.28	34	31.2	41	21.7	1.54	0.90, 2.66
Missing data	0		1				2		0			
Hysterectomy												
No	537	72.2	667	76.9	1.00	Referent	82	73.9	145	76.7	1.00	Referent
Yes	207	27.8	200	23.1	1.22	0.97, 1.54	29	26.1	44	23.3	1.07	0.61, 1.87
Missing data	2		1				0		0			
History of infertility												
No	651	87.3	783	90.2	1.00	Referent	102	91.9	175	92.6	1.00	Referent
Yes	95	12.7	85	9.8	1.38	1.01, 1.89	9	8.1	14	7.4	1.13	0.47, 2.73
Missing data	0		0				0		0			
History of endometriosis												
No	650	87.7	793	92.3	1.00	Referent	109	98.2	184	98.4	1.00	Referent
Yes	91	12.3	66	7.7	1.76	1.26, 2.46	2	1.8	3	1.6	1.16	0.19, 7.08
Missing data	5		9				0		2			
First-degree family history of breast or ovarian cancer												
No	582	78.1	720	83.1	1.00	Referent	69	62.2	159	84.1	1.00	Referent
Yes	163	21.9	146	16.9	1.33	1.04, 1.71	42	37.8	30	15.9	3.15	1.82, 5.45
Missing data	1		2				0		0			
Talc use												
No	328	59.6	325	61.0	1.00	Referent	45	54.2	75	56.0	1.00	Referent
Yes	222	40.4	208	39.0	1.04	0.82, 1.33	38	45.8	59	44.0	1.19	0.68, 2.09
Missing data	196		335				28		55			
Body mass index[b] 1 year before diagnosis or interview												
<25	312	43.3	369	43.7	1.00	Referent	17	15.9	31	17.1	1.00	Referent
25–<30	212	29.4	256	30.3	0.96	0.76, 1.22	26	24.3	58	32.0	0.84	0.39, 1.78
30–<35	114	15.8	124	14.7	1.08	0.80, 1.45	22	20.6	43	23.8	0.94	0.43, 2.07
≥35	83	11.5	95	11.3	1.04	0.75, 1.45	42	39.3	49	27.1	1.62	0.79, 3.35
Missing data	25		24				4		8			
Height, m												
<1.6	195	26.2	242	27.9	1.00	Referent	25	22.7	57	30.2	1.00	Referent
1.6–<1.7	430	57.8	483	55.8	1.13	0.90, 1.42	64	58.2	102	54.0	1.48	0.84, 2.62
≥1.7	119	16.0	141	16.3	1.11	0.81, 1.51	21	19.1	30	15.9	1.74	0.83, 3.65
Missing data	2		2				1		0			

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Adjusted for age.
[b] Weight (kg)/height $(m)^2$.

and whites. Unconditional logistic regression analyses were used to calculate age-adjusted and multivariable-adjusted odds ratios and 95% confidence intervals separately for each racial/ethnic group. Variables included in the race/ethnicity-specific multivariable models were age, age at menarche, number of pregnancies, duration of oral contraceptive use, history of tubal ligation, family history of breast and ovarian cancer, and body mass index (BMI; weight (kg)/height $(m)^2$). The variables included in multivariable models were selected a priori and included the most well-established risk

factors for ovarian cancer as well as BMI, because of the pronounced racial/ethnic differences in the prevalence of obesity. We also conducted multivariable analyses limited to parous women that included all of the above variables plus breastfeeding. Finally, to test for interactions, we fitted models for women of both racial/ethnic groups combined which included a term for race/ethnicity and product terms for race/ethnicity × age at menarche, race/ethnicity × breastfeeding, and race/ethnicity × family history of breast or ovarian cancer.

Population attributable fractions were calculated using the method described by Bruzzi et al. (13) for the potentially modifiable factors tubal ligation (yes vs. no), oral contraceptive use (≥1 year vs. <1 year), history of pregnancy (ever vs. never), and BMI (<30 vs. ≥30). For these analyses, the reference categories were assigned to the lower risk category (i.e., having had a tubal ligation, oral contraceptive use for ≥1 year, ever being pregnant, and BMI <30) so the attributable fraction could be interpreted as the proportion of cases that theoretically could be eliminated if all women in the population were shifted to the low risk category.

RESULTS

The tumor characteristics of the ovarian cancer cases are presented in Table 1 by race/ethnicity. The proportions of cases that were invasive were similar for African Americans and whites (78% and 79%, respectively). Because low-malignant-potential ovarian cancer may be etiologically distinct from invasive cancer (14, 15), we focused the remainder of our analyses on invasive disease. Among invasive cases, the most important histologic differences were that tumors in African Americans were less likely to be clear-cell and more likely to be of a histologic type other than the 4 primary types (serous, endometrioid, mucinous, and clear-cell). African-American women were more likely to be diagnosed with higher-stage disease and somewhat less likely to have poorly differentiated tumors, although the differences in grade were not statistically significant.

Comparisons of risk factors for ovarian cancer among African-American and white women are presented in Table 2. Because age-matching was based on all cases but this analysis was restricted to invasive cases, who are on average older than low-malignant-potential cases, the age distribution of the controls was slightly younger than that of the cases.

In age-adjusted analyses, many of the major reproductive factors that have been associated with ovarian cancer risk among white women were similarly related to risk among African-American women. Women who were parous, had a later age at last pregnancy, had used oral contraceptives for 1 year or more, or had had a tubal ligation were at reduced risk of invasive ovarian cancer; however, there was not strong evidence of a linear relation with number of pregnancies for African-American women. History of infertility or endometriosis was associated with a significantly increased risk for white women and a modestly but not significantly increased risk for African-American women. Family history of breast or ovarian cancer in a first-degree relative was associated with increased risk in both racial/ethnic groups, with a stronger association among African Americans. Later age at menarche and history of ever breastfeeding were associated with reduced risk in white women, whereas no association was observed among African Americans. Analyses of anthropometric characteristics suggested that taller height and BMI ≥35 may be associated with risk among African-American women but not among white women.

In multivariable models (Table 3), results were generally similar to those observed in the age-adjusted models. The association with age at menarche ≥12 years appeared to differ by race/ethnicity, with an odds ratio of 1.30 (95% confidence interval (CI): 0.67, 2.53) for African Americans rather than the expected inverse association. The strength of the association with family history of breast or ovarian cancer also appeared to differ by race/ethnicity. *P* values for the interaction terms were 0.032 for race/ethnicity × family history and 0.068 for race/ethnicity × age at menarche. In models limited to parous women that included all of the variables in Table 3 plus history of breastfeeding, white women who had breastfed had a nonsignificantly reduced risk (odds ratio = 0.83, 95% CI: 0.65, 1.06), whereas there was no suggestion of a protective effect among African-American women (odds ratio = 1.09, 95% CI: 0.57, 2.07).

In addition to some differences between African Americans and whites in the magnitude of associations with certain risk factors, there were marked racial/ethnic differences in the prevalences of a number of risk factors considered. For example, prevalences in African-American and white controls, respectively, were 29% and 18% for age at menarche less than 12 years, 6% and 10% for nulligravidity, 51% and 33% for tubal ligation, and 51% and 26% for BMI ≥30 (Table 3). We therefore hypothesized that the relative contribution of established risk factors for ovarian cancer could vary considerably between African Americans and whites. To address this, we calculated population attributable fractions for the potentially modifiable risk factors of pregnancy, oral contraceptive use, BMI, and tubal ligation. As Table 4 shows, the attributable fractions for not having a tubal ligation, high BMI, and no oral contraceptive use were considerably higher for African Americans than for whites, reflecting the stronger associations and/or higher prevalence of these factors among African Americans.

DISCUSSION

Our analyses of ovarian cancer risk factors in African-American and white women show similar relations for several characteristics, including inverse associations with parity, oral contraceptive use, and tubal ligation, but there are also suggestions of racial/ethnic differences in either the direction or the magnitude of association for other risk factors. History of breastfeeding and later age at menarche were both associated with reduced risk among whites, whereas these associations were absent among African Americans. Family history of breast or ovarian cancer was associated with increased risk for both African Americans and whites, but the association was considerably stronger for African-American women. We considered the possibility that the

Table 3. Odds Ratios for Invasive Epithelial Ovarian Cancer (Multivariable Logistic Regression Models) in African-American and White Women, North Carolina Ovarian Cancer Study, 1999–2008

	Whites						African Americans					
	Cases		Controls		OR[a]	95% CI	Cases		Controls		OR[a]	95% CI
	No.	%	No.	%			No.	%	No.	%		
Age, years (continuous variable)	715		837		1.01	1.00, 1.02	106		181		1.00	1.00, 1.02
No. of pregnancies												
0	114	15.9	84	10.0	1.00	Referent	14	13.2	11	6.1	1.00	Referent
1–2	306	42.8	332	39.7	0.66	0.47, 0.94	29	27.4	68	37.6	0.28	0.09, 0.86
≥3	295	41.3	421	50.3	0.46	0.32, 0.65	63	59.4	102	56.4	0.52	0.17, 1.62
Age at menarche, years												
<12	172	24.1	151	18.0	1.00	Referent	26	24.5	52	28.7	1.00	Referent
≥12	543	75.9	686	82.0	0.65	0.50, 0.84	80	75.5	129	71.3	1.30	0.67, 2.53
Tubal ligation												
No	535	74.8	561	67.0	1.00	Referent	73	68.9	89	49.2	1.00	Referent
Yes	180	25.2	276	33.0	0.74	0.58, 0.94	33	31.1	92	50.8	0.43	0.24, 0.80
Duration of oral contraceptive use, years												
Never use	233	34.1	225	27.6	1.00	Referent	45	43.3	55	32.0	1.00	Referent
<1	95	13.9	88	10.8	1.18	0.82, 1.69	15	14.4	14	8.1	1.89	0.73, 4.95
1–<5	162	23.7	222	27.2	0.78	0.58, 1.05	23	22.1	55	32.0	0.72	0.34, 1.53
≥5	193	28.3	281	34.4	0.73	0.54, 0.97	21	20.2	48	27.9	0.52	0.24, 1.15
Missing data	32		21				2		9			
Family history of breast or ovarian cancer												
No	559	78.2	697	83.3	1.00	Referent	66	62.3	153	84.5	1.00	Referent
Yes	156	21.8	140	16.7	1.31	1.00, 1.72	40	37.7	28	15.5	2.73	1.45, 5.14
Body mass index[b] 1 year before diagnosis/ interview												
<25	309	43.2	368	44.0	1.00	Referent	17	16.0	31	17.1	1.00	Referent
25–<30	211	29.5	254	30.3	0.92	0.71, 1.18	26	24.5	58	32.0	0.96	0.40, 2.30
30–<35	112	15.7	122	14.6	1.17	0.85, 1.61	22	20.8	43	23.8	1.32	0.53, 3.26
≥35	83	11.6	93	11.1	1.03	0.72, 1.47	41	38.7	49	27.1	1.52	0.65, 3.56

Abbreviations: CI, confidence interval; OR, odds ratio.
[a] Adjusted for all of the variables in the table.
[b] Weight (kg)/height $(m)^2$.

stronger association in African-American women was due to inaccurate reporting; however, the prevalences of a family history of breast or ovarian cancer were very similar among African-American and white controls, which argues against there being differential reporting of family history across racial/ethnic groups.

Although these observed racial/ethnic differences in the magnitude or direction of associations with established ovarian cancer risk factors are intriguing, the limitations of our analyses must be acknowledged. The North Carolina Ovarian Cancer Study included more African-American women than any other study of ovarian cancer, but the relatively small sample made it difficult to ascertain which associations were true associations and which were chance findings.

The modest sample size also precluded us from conducting analyses within subgroups defined by either menopausal status or histologic type. Several reports have suggested that reproductive risk factors and high BMI are more strongly associated with premenopausal disease (16–23). However, with only 38 premenopausal African-American cases in our study population, analyses stratified by menopausal status would not have yielded meaningful results. Similarly, the sample was too small for us to explore differences in risk factors by histologic subtype. The relatively small number of African-American cases also led us to dichotomize some

Table 4. Odds Ratios for Invasive Epithelial Ovarian Cancer and Population Attributable Fractions for Selected Ovarian Cancer Risk Factors in African-American and White Women, North Carolina Ovarian Cancer Study, 1999–2008

	Whites					African Americans				
	No. of Cases	No. of Controls	OR[a]	95% CI	AF	No. of Cases	No. of Controls	OR[a]	95% CI	AF
Tubal ligation										
Yes	168	269	1.00	Referent	0.204	33	91	1.00	Referent	0.341
No	515	547	1.37	1.08, 1.73		71	81	2.00	1.15, 3.48	
Body mass index[b]										
<30	494	611	1.00	Referent	0.030	42	86	1.00	Referent	0.209
≥30	183	205	1.12	0.89, 1.42		62	86	1.54	0.91, 2.62	
Duration of oral contraceptive use, years										
≥1	355	503	1.00	Referent	0.119	44	103	1.00	Referent	0.245
<1	328	313	1.33	1.06, 1.67		60	69	1.74	0.99, 3.05	
Ever being pregnant										
Yes	575	734	1.00	Referent	0.052	91	164	1.00	Referent	0.079
No	108	82	1.49	1.06 2.08		14	8	2.43	0.88, 6.73	

Abbreviations: AF, attributable fraction; CI, confidence interval; OR, odds ratio.

[a] Adjusted for all of the variables in the table, as well as age, age at menarche, family history of breast or ovarian cancer, and breastfeeding.

[b] Weight (kg)/height $(m)^2$.

variables of interest in our analyses and dictated that we limit the number of potential confounders evaluated in our multivariable models. A larger sample would have afforded us the opportunity to further explore the effects of the timing and duration of oral contraceptive use and the timing of pregnancies or tubal ligation.

Additional limitations of our analysis included those related to the case-control method. The possibility of bias being introduced due to nonparticipation of ovarian cancer cases and controls should be considered. Although we used rapid case ascertainment to identify cases within 2 months of diagnosis and the median time to case interview was 4.5 months, which should have minimized survival bias, there is a possibility that cases who participated differed from those who did not. When we compared the tumor characteristics of ovarian cancer cases who were identified as eligible but did not participate (because of death, lack of physician consent, participant refusal, or inability to contact them) with the tumor characteristics of cases who did participate, we found that the proportion of invasive cases was slightly smaller among participants than among nonparticipants. This is not a surprising finding, given that cases who died quickly or for whom physicians did not give consent were more likely to have advanced disease. Among the invasive cases that were the focus of most of our analyses, we found no statistically significant differences in the proportions of higher-stage cancers between participants and nonparticipants. The racial/ethnic differences in histologic type that we observed among participants (i.e., a lower proportion of clear-cell tumors and a higher proportion of tumors of "other" histologic types among African Americans) were also observed among the nonparticipating cases. Thus, the invasive cases enrolled in the study appeared to be representative of the ovarian cancer cases diagnosed in our catchment area.

Nonparticipation also has the potential to introduce bias if participating cases and controls differ from persons who decline to participate in the study. Although we had no risk factor information on nonparticipants with which to assess their similarity with women who participated in the study, the associations we observed for white women within our study population are consistent with established ovarian cancer risk factors, which argues against our results' being biased due to nonparticipation.

Despite the limited sample of African-American women, the descriptive characteristics of our population and the attributable fraction analyses suggest that the relative importance of ovarian cancer risk factors may vary between African Americans and whites because of the substantial differences in the prevalence and strength of associations with factors such as tubal ligation and obesity. Tubal ligation, which had a stronger association with ovarian cancer among African Americans and is considerably more common among African Americans in our study population as well as in national surveys (6), could be an important explanatory factor for the lower rates of ovarian cancer among African Americans.

Obesity, which has shown modest associations with ovarian cancer risk in the majority of studies (22, 24–26), may be a considerably more important risk factor for African-American women, as evidenced by the markedly higher attributable fraction for obesity that we observed in our data. Consistent with national statistics (12), our data showed a much higher prevalence of obesity among African Americans than among whites. In particular, severe obesity

(BMI ≥35), which had a threefold higher prevalence among African Americans than among whites in our study, may be especially relevant as a risk factor for ovarian cancer among African Americans. Some investigators have reported either that associations between BMI and ovarian cancer risk were present only for persons with very high BMIs or that the relations were considerably stronger for women in the highest BMI categories (27, 28). Other investigators have found that the association between obesity and ovarian cancer was present only among premenopausal women or was much stronger for premenopausal ovarian cancer than for postmenopausal ovarian cancer (21, 22). Because the markedly higher prevalence of obesity among African-American women is apparent even among adults aged 20–39 years (12), African-American women may be at higher risk for ovarian cancer diagnosed at a younger age. This is consistent with the higher proportion of premenopausal ovarian cancer cases in African Americans as compared with whites (34% vs. 26%) and the younger mean age at diagnosis (54.8 years vs. 57.4 years) that we observed in our population and that has been reported in Surveillance, Epidemiology, and End Results data (1). The younger age at diagnosis also may be related to the stronger association with family history of breast or ovarian cancer among African-American women, which could be indicative of higher genetic risk.

Our data suggest that the relative importance of ovarian cancer risk factors may vary between African-American and white women because of differences in the prevalence of and strength of associations with characteristics such as tubal ligation, pregnancy, and obesity. However, conclusions that can be drawn from our data are limited by the small number of African Americans in our analysis, despite our study population's having more African-American women than any other existing study of ovarian cancer. Because ovarian cancer is a leading cause of cancer mortality in African Americans, there is a clear need for additional studies in order to deepen our understanding of causative and protective factors in this population.

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